On a broader note, Dr Noel highlights a point with which we could not agree with more: national self-sufficiency in organ transplantation is needed to combat organ tourism and achieve global justice in transplantation. As the Declaration of Istanbul on Organ Trafficking and Transplant Tourism suggests, national governments have a responsibility to monitor their transplant activity, prohibiting unethical transplant practices.[3]

1. Nöel L. The data on transplantation in Saudi Arabia are complex and require additional framework for interpretation. *Kidney Int* 2009; **76**: 914.
2. Horvat LD, Shariff SZ, Garg AX. Global trends in the rates of living kidney donation. *Kidney Int* 2009; **75**: 1088–1098.
3. International Summit on Transplant Tourism and Organ Trafficking. The Declaration of Istanbul on Organ Trafficking and Transplant Tourism. *Clin J Am Soc Nephrol* 2008; **3**: 1227–1231.

Lucy D. Horvat[1,2] and Amit X. Garg[1,2]
[1]*Division of Nephrology, Department of Medicine, University of Western Ontario, London, Canada and* [2]*London Kidney Clinical Research Unit, Department of Epidemiology and Biostatistics, University of Western Ontario, London, Canada*
Correspondence: *Amit X. Garg, London Kidney Clinical Research Unit, Department of Epidemiology and Biostatistics, London Health Sciences Centre, University of Western Ontario, Room ELL-101, Westminster Tower, 800 Commissioners Road East, London, Ontario, Canada N6A 4G5. E-mail: amit.garg@lhsc.on.ca*

Mineral complexes and vascular calcification

Kidney International (2009) **76,** 915; doi:10.1038/ki.2009.273

To the Editor: Matsui *et al.*[1] have nicely demonstrated a fetuin-containing mineral complex in adenine-treated rats with renal failure that is prevented by alendronate treatment. However, the conclusion that this is related to, or is a marker of vascular calcification is premature. The presence of this complex is not surprising considering the extremely high circulating phosphate levels that occur in this model. In addition, the failure to control pH during the preparation of the serum almost certainly increased these complexes because of the reduced solubility in alkaline solution. We routinely dilute our plasma samples immediately after they are obtained in order to prevent precipitation of calcium and phosphate. The absence of the complexes in alendronate-treated rats can easily be explained by the significantly lower calcium concentration, which, as was shown by the authors, has a major impact on complex formation. The inhibition of vascular calcification is probably due to a direct inhibition as we have shown for bisphosphonates in cultured aortas.[2] The formation of the mineral complexes is probably just a physicochemical phenomenon related to ambient phosphate and calcium levels. Their correlation with vascular calcification can be explained by the fact that calcium and phosphate levels also affect vascular calcification, rather than by a direct pathophysiological link.

1. Matsui I, Hamano T, Mikami S *et al.* Fully phosphorylated fetuin-A forms a mineral complex in the serum of rats with adenine-induced renal failure. *Kidney Int* 2009; **75**: 915–918.
2. Lomashvili KA, Monier-Faugere M-C, Wang X *et al.* Effect of bisphosphonates on vascular calcification and bone metabolism in experimental renal failure. *Kidney Int* 2009; **75**: 617–625.

W. Charles O'Neill[1]
[1]*Emory University, Renal Division, WMB 338, Atlanta, Georgia, USA*
Correspondence: *W. Charles O'Neill, Emory University, Renal Division, WMB 338, 1639 Pierce Dr, Atlanta, GA 30322, USA. E-mail: woneill@emory.edu*

Response to 'Mineral complexes and vascular calcification'

Kidney International (2009) **76,** 915–916; doi:10.1038/ki.2009.278

We thank Dr O'Neill for his interest in our study and his comments[1] on our article.

We previously showed that serum fetuin-A concentrations were not significantly associated with coronary artery calcification scores in diabetic chronic kidney disease patients.[2] Therefore, we tried to elucidate whether low serum fetuin-A levels really correlate with vascular calcification in animal models. Renal failure model rats showed that not serum fetuin-A concentrations but fetuin–mineral complex (FMC) correlated with the extent of vascular calcification.[3] This complex was not observed in rats without vascular calcification. As we only found the association between FMC and vascular calcification in rats with adenine-induced renal failure, further investigation must be carried out to assert that FMC is a marker of vascular calcification stress.

Serum pH levels might affect FMC formation. As we did not control pH during serum preparation,[3] we measured the pH of residual serum samples. Serum pH was 7.762 ± 0.119 in control rats, 7.691 ± 0.088 in adenine rats at 2 weeks, 7.583 ± 0.045 at 4 weeks, and 7.614 ± 0.062 at 5 weeks. Although the addition of 1 M Tris-HCl (pH 7.2) to these serum samples decreased pH, we found similar FMC in pH-modified adenine rat serum (data not shown). This preliminary result suggests that FMC can exist in serum without alkalemia.

We showed that injection of alendronate to adenine rats reduced FMC, followed by the inhibition of vascular calcification. Lomashvili *et al.*[4] demonstrated well the mechanism by which bisphosphonates prevent medial vascular calcification. They showed that etidronate and pamidronate can directly inhibit vascular calcification independent of bone resorption.[4] It is possible that alendronate also directly functioned in our model. However, the changes in serum/plasma calcium levels by bisphosphonate administration suggest another mechanism. Alendronate decreased serum calcium in our experiment, but etidronate and pamidronate did not in Lomashvili's experiments,[4] except for the highest etidronate group. This difference may indicate that bone

resorption of our animal model was further repressed than those used in Lomashvili's experiments.[4]

The mechanism of FMC generation remains uncertain. Although the formation of FMC might be just a physicochemical phenomenon related to ambient phosphate and calcium levels, we speculate that some other factors should participate in FMC formation because of the following two findings. First, using mass spectrometry, we found similar FMC in the serum of a hemodialysis patient whose adjusted serum calcium and phosphate levels were only 10.6 mg per 100 ml and 6.0 mg per 100 ml, respectively. Second, the maneuver of centrifugation reduced the level of fetuin-A from 0.807 g/l to 0.211 g/l in the sera of 20 diabetic chronic kidney disease stage 4 patients who had coronary artery calcification detected by computed tomography, suggesting the presence of FMC even in normal ranges of calcium and phosphate. (Mikami *et al.* American Society of Nephrology 2007 presentation; *J Am Soc Nephrol* 18. 747A, 2007).

1. O'Neill WC. Mineral complexes and vascular calcification. *Kidney Int* 2009; **76**: 915.
2. Mikami S, Hamano T, Fujii N *et al.* Serum osteoprotegerin as a screening tool for coronary artery calcification score in diabetic pre-dialysis patients. *Hypertens Res* 2008; **31**: 1163–1170.
3. Matsui I, Hamano T, Mikami S *et al.* Fully phosphorylated fetuin-A forms a mineral complex in the serum of rats with adenine-induced renal failure. *Kidney Int* 2009; **75**: 915–928.
4. Lomashvili KA, Monier-Faugere MC, Wang X *et al.* Effect of bisphosphonates on vascular calcification and bone metabolism in experimental renal failure. *Kidney Int* 2009; **75**: 617–625.

Isao Matsui[1], Takayuki Hamano[1], Satoshi Mikami[1], Yoshitaka Isaka[1] and Hiromi Rakugi[1]

[1]*Department of Geriatric Medicine and Nephrology, Osaka University, Suita, Osaka, Japan*

Correspondence: *Takayuki Hamano, Osaka University, Geriatric Medicine and Nephrology, 2-2, Yamadaoka, Suita, Osaka 565-0871, Japan.*
E-mail: hamatea@medone.med.osaka-u.ac.jp

Enterovesical fistula and roundworms

Kidney International (2009) **76,** 916; doi:10.1038/ki.2009.276

Gupta *et al.*[1] describe a man with urinary obstruction due to the presence of *Ascaris lumbricoides*. No further investigation was conducted to determine why such roundworms were present in the urinary system. The life cycle of *A. lumbricoides* in humans is spent only in respiratory and gastrointestinal tracts.[2] Enterovesical fistula is possible, and the common causes for such fistulas, e.g. colon cancer and sigmoid diverticulitis, may present in the patient.[3] Failure to perform further investigations on this aspect would delay the diagnosis and management of a treatable disorder.

1. Gupta P, Sundaram V, Abraham G *et al.* Obstructive uropathy from *Ascaris lumbricoides*. *Kidney Int* 2009; **75**: 1242.
2. Ascariasis. http://www.dpd.cdc.gov/dpdx/html/Ascariasis.htm (accessed 15 May 2009).
3. Naguib NN, Sharaf UI. Vesicorectal fistula, case report and review of literature. *Curr Urol* 2008; **2**: 211–213.

Weekitt Kittisupamongkol[1]

[1]*Faculty of Medicine, Chulalongkorn University, Patumwan, Bangkok, Thailand*

Correspondence: *Weekitt Kittisupamongkol, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand.*
E-mail: weekitti@gmail.com

Complications impair the usefulness and validity of the rat tail arteriovenous fistula model

Kidney International (2009) **76,** 916; doi:10.1038/ki.2009.311

To the Editor: We wish to follow up the report of a new rat tail model of the hemodialysis arteriovenous fistula (AVF).[1] Such models are potentially important because maturation failure of AVFs is a major unsolved problem. Lin *et al.*[1] reported 5/5 successful operations in which the lateral vein was anastomosed end-to-side to the ventral artery. We report our experience in creating 27 such AVFs.

We have found that technical problems limit the usefulness of this model. Sample tail fistulas were dissected several weeks after AVF, and dense scar tissue (adhesions) encased the arteries and veins. These adhesions compressed the vessels and likely altered the flow characteristics. Other obstacles encountered included thrombosis and dessication. We found that systemic heparinization before the procedure and minimization of vessel occlusion time reduced the risk of thrombosis. Compromise of the wound closure, anastamotic compression, and alteration of blood vessel elasticity resulted when meticulous attention was not paid to ensuring that the tissue was sufficiently moist.

We concur that the tail fistula is technically feasible; however, a technically successful tail fistula is subjected to external forces that compromise flow characteristics, thereby calling into question the validity of this model. Turbulence and low shear stress are believed to induce stenosis in AVFs, rendering adhesion avoidance crucial to the application of the tail fistula as a model of hemodialysis access dysfunction.

1. Lin T, Horsfield C, Robson M. Arteriovenous fistula in the rat tail: a new model of hemodialysis access dysfunction. *Kidney Int* 2008; **74**: 528–531.

John S. Beatty[1], Paul F. Wach[2], William D. Paulson[3], Todd D. Merchen[1], David M. Pollock[2], Jennifer S. Pollock[2] and John J. White[3]

[1]*Department of Surgery, Medical College of Georgia, Augusta, Georgia, USA;* [2]*Vascular Biology Center, Medical College of Georgia, Augusta, Georgia, USA and* [3]*Department of Nephrology, Medical College of Georgia, Augusta, Georgia, USA*

Correspondence: *John S. Beatty, Medical College of Georgia, Department of Surgery, 1120 15th Street, BB 4516, Augusta, Georgia, 30912, USA.*
E-mail: jbeatty@mcg.edu